



## PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 101285-1 WO	<b>FOR FURTHER ACTION</b> See Form PCT/IPEA/416	
International application No. PCT/GB2004/004650	International filing date (day/month/year) 04.11.2004	Priority date (day/month/year) 07.11.2003
International Patent Classification (IPC) or national classification and IPC INV. A61K31/445 A61K31/4535 A61K31/4525 A61K31/4545 C07D211/32 C07D409/06 C07D405/06 C07D401/06 C07D417/06 A61P3/10		
Applicant ASTRAZENECA AB		
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>		
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input checked="" type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>		
Date of submission of the demand  12.08.2005	Date of completion of this report  15.05.2006	
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Kollmannsberger, M  Telephone No. +49 89 2399- 	

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**Box No. I Basis of the report**

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1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4)
  - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements\*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

**Description, Pages**

1-45 as originally filed

**Claims, Numbers**

1-31 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing *(specify):*
  - ☐ any table(s) related to sequence listing *(specify):*
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing *(specify):*
  - ☐ any table(s) related to sequence listing *(specify):*

\* If item 4 applies, some or all of these sheets may be marked "superseded."

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

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1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 31

because:

☒ the said international application, or the said claims Nos. 31 relate to the following subject matter which does not require an international preliminary examination (specify):

**see separate sheet**

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	23-26
	No: Claims	1-22,27-31
Inventive step (IS)	Yes: Claims	23-26
	No: Claims	1-22,27-31
Industrial applicability (IA)	Yes: Claims	1-30
	No: Claims	

2. Citations and explanations (Rule 70.7):

**see separate sheet**

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**Box No. VI Certain documents cited**

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1. Certain published documents (Rule 70.10)

and /or

2. Non-written disclosures (Rule 70.9)

**see separate sheet**

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claim 31 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**V-1. Prior art:**

The following documents are considered relevant:

- D1: WO 2004/089470 A2 (NOVO NORDISK A/S; ANDERSEN, HENRIK, SUNE; KAMPEN, GITA, CAMILLA, TEJLG) 21 October 2004 (2004-10-21)
- D2: WO 2004/033427 A1 (ASTRAZENECA AB; ASTRAZENECA UK LIMITED; BARTON, PETER, JOHN; JEWSBURY,) 22 April 2004 (2004-04-22)
- D3: WO 03/072197 A1 (PFIZER PRODUCTS INC; PERRY, DAVID, AUSTEN; HARWOOD, HAROLD, JAMES, JR) 4 September 2003 (2003-09-04)
- D4: ORJALES, AURELIO ET AL: "Syntheses and Binding Studies of New [(Aryl)(aryloxy)methyl]piperidine Derivatives and Related Compounds as Potential Antidepressant Drugs with High Affinity for Serotonin (5-HT) and Norepinephrine (NE) Transporters" JOURNAL OF MEDICINAL CHEMISTRY , 46(25), 5512-5532 CODEN: JMCMAR; ISSN: 0022-2623, 1 November 2003 (2003-11-01), XP002315824
- D5: PATEL, HARSHADKUMAR ET AL: "Mechanism and stereochemistry of formation and cleavage of epoxy ethers. III" JOURNAL OF ORGANIC CHEMISTRY , 30(12), 4337-8 CODEN: JOCEAH; ISSN: 0022-3263, 1965, XP002315825
- D6: EP-A-0 378 207 (TAKEDA CHEMICAL INDUSTRIES, LTD) 18 July 1990 (1990-

07-18)

- D7: DATABASE CAPLUS [Online] CHEMICAL ABSTRACTS SERVICE,  
COLUMBUS, OHIO, US; LYLE, ROBERT E. ET AL: "The synthesis of potential  
medicinal agents from 1-methyl-3-bromo-3-piperidyl phenyl ketone"  
XP002315826 retrieved from STN Database accession no. 1961:112121
- D8: WO 01/21577 A2 (TAKEDA CHEMICAL INDUSTRIES, LTD; KATO,  
KANEYOSHI; TERAUCHI, JUN; MORI,) 29 March 2001 (2001-03-29)
- D9: DATABASE CAPLUS [Online] CHEMICAL ABSTRACTS SERVICE,  
COLUMBUS, OHIO, US; "Piperidines" XP002315827 retrieved from STN  
Database accession no. 1986:207174
- D10: WO 03/065983 A2 (MERCK & CO., INC; BALKOVEC, JAMES, M;  
THIERINGER, ROLF; MUNDT, STEVEN,) 14 August 2003 (2003-08-14)

D1 and D2 are P-documents and will be disregarded during the PCT procedure.

V-2. Novelty (Art. 33(2) PCT):

D3 discloses compounds (cf. e. g. examples 5, 6 and many others) which are included in the compounds (I) according to present claim 1 for X=bond, Y=heterocyclyl, R2=C1-alkanoyl substituted by carbocyclic or heterocyclic groups (as R6). These compounds are used to treat metabolic syndrome (cf. page 1 lines 1-6). D1 is thus novelty destroying for independent claims 1, 27 and 31. Since the specific cyclic groups for A as defined in claim 13 are not disclosed in D1, claim 13 is not affected.

D4 and D5 disclose compounds included in the definition of claim 13 (see compounds indicated in the search report). Since these documents do not mention medical uses of the disclosed compounds, claims 24-26 are not affected

D6-D9 disclose compounds included in the proviso of claim 13. D10 discloses triazoles instead of piperidines.

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The independent claims are thus not novel. Since the example compounds of claim 23 are not specifically disclosed in the cited documents, claim 23 is novel.

**V-3. Inventive step (Art. 33(3) PCT):**

Since the independent claims are not novel also Art. 33(3) PCT is not fulfilled. For novel parts of the claims D10 forms the closest state of the art since D10 discloses inhibitors of the same enzyme 11-beta-hydroxysteroid dehydrogenase type 1. Since the compounds of D10 are structurally remote, novel parts of the claims fulfil Art. 33(3) PCT.

**Re Item VI**

**Certain documents cited**

**Certain published documents**

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO2004/089470	21 October 2004	6 April 2004	11 April 2003
WO2004033427	22 April 2004	7 October 2003	11 October 2002